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EXERCISE FOR DEMENTIA AND MILD COGNITIVE IMPAIRMENT: METHODOLOGICAL CONSIDERATIONS

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ABSTRACT

The exponential worldwide increase in the number of older adults is causing a parallel rise in the number of cases of neurodegenerative diseases, such as mild cognitive impairment (MCI) and dementia. Exercise is a promising strategy for improving physical and cognitive function in healthy older adults, reducing the risk of developing MCI and dementia, and improving physical and cognitive function as well as decreasing neuropsychiatric symptoms in people with MCI and dementia. However, there are still some inconsistencies in the literature, especially in regards to the cognitive benefits, and there are currently no guidelines for prescribing exercise for older adults with cognitive impairment. In this article, a narrative review on the benefits of exercise for people with MCI and dementia was conducted, establishing some preliminary guidelines for prescribing exercise efficiently and safely in this population.

Keywords: exercise, dementia, cognitive impairment, older adults

EJERCICIO FÍSICO PARA PERSONAS CON DEMENCIA Y DETERIORO COGNITIVO LEVE: CONSIDERACIONES METODOLÓGICAS

RESUMEN

El incremento exponencial del número de personas mayores a nivel mundial, está causando un aumento paralelo en el número de casos de enfermedades neurodegenerativas, como es el caso del deterioro cognitivo leve (DCL) o la demencia. El ejercicio físico es una estrategia prometedora para mejorar la función física y cognitiva de los adultos mayores sanos, reducir el riesgo de desarrollar un DCL o una demencia, así como mejorar la función física, cognitiva y los síntomas neuropsiquiátricos en personas con DCL o demencia. Sin embargo, existen todavía algunas inconsistencias en la literatura científica, especialmente acerca de los beneficios cognitivos, y faltan pautas metodológicas para prescribir ejercicio físico para personas mayores con deterioro cognitivo. En este artículo, se ha llevado a cabo una revisión narrativa de la literatura acerca de los beneficios del ejercicio físico para personas con DCL y demencia, estableciendo unas pautas metodológicas preliminares para prescribir ejercicio físico, de forma eficiente y segura en esta población.

Palabras clave: ejercicio físico, demencia, deterioro cognitivo, personas mayores

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INTRODUCTION

An extended average life expectancy is causing a significant increase in the population of persons aged 65 or older. This exponential increase in older adults will cause a parallel increase in the number of cases of neurodegenerative diseases such as dementia (Haan & Wallace, 2004). According to the Diagnostic Statistic Manual of Mental Disorders (DSM-5) (APA, 2013), dementia is the term that refers to several disorders characterised by the development of multiple cognitive deficits, including memory loss and at least one of the following cognitive problems: aphasia (language problems), apraxia (motor function problems), agnosia (sensory problems) or executive function deficits (planning, organisation, sequencing, abstract thought, etc.). Prince et al. (2013) calculated that the total number of cases of dementia will double every twenty years reaching 65.7 million in 2030 and 115.4 in 2050.

There are several types of dementia such as Alzheimer´s disease (AD) or vascular dementia. AD is the most prevalent subtype representing 60% to 80% of the total cases. It destroys the brain cells, causing a progressive deterioration in several cognitive functions such as memory, problem solving, spatial orientation and thought (Rimmer & Smith, 2009). A deterioration of executive functions is also a common characteristic of dementia, and has as a consequence apathy, lack of motivation and agitation, which has been shown to predict progression from amnestic mild cognitive impairment (a-MCI) to AD (Marshall et al., 2011).

AD also causes mood disorders, deterioration of physical function such as in gait, coordination and balance (Buchman et al., 2009), as well as problems in performing activities of daily living (ADL) (Onor et al., 2007; Rimmer & Smith, 2009). Furthermore, this pathology has devastating consequences for the caregivers as well.

The projected costs for the care of the growing number of people with dementia are discouraging. The total cost of dementia worldwide increased from 604,000 million dollars in 2010 to 818,000 million in 2015, which represents a 35.4% increase. They estimated that the total cost will exceed 1 billion dollars in 2018 and reach 2 billion in 2030. Western Europe and North America account for 70% of these costs (Prince et al., 2015).

Although dementia cannot be cured, the symptoms associated with the disease can be influenced (Blankevoort et al., 2010). Considering the projected number of cases and the personal, social and economic consequences of dementia, it is imperative to design strategies to prevent and treat this disease. Early detection of the pathology may offer an opportunity for prevention. In the context of dementia, MCI represents this early stage and it is, thus, considered of special interest for developing prevention strategies (Petersen et al., 2009).

MCI involves a higher decline in cognitive abilities than would be normally expected by the person´s age and education level but not severe enough yet to meet criteria for a diagnosis of dementia. There are several types of MCI, including amnestic, non-amnestic and single or multiple domain. MCI of the amnestic type includes memory loss and is considered as a transition stage between normal aging and AD (Petersen, 2004).

Pharmacologic treatments for dementia and MCI have not been successful so far for either cognitive improvement or reduction of incident dementia and its severity. Thus, nonpharmacologic interventions addressing cognitive decline and general quality of life are especially needed. These strategies may include diet, cognitive stimulation, recreational therapy or/and physical activity and exercise (Tortosa-Martínez & Yoder, 2015)

Exercise seems to improve cognitive function in healthy older adults (Erickson et al., 2011; Kramer & Erickson, 2007) as well as to prevent MCI and dementia (Geda et al., 2010; Hamer & Chida, 2009). Furthermore, there is increasing evidence showing that exercise is beneficial for patients with MCI and dementia in physical function, cognition and neuropsychiatric symptoms, as summarized below.

Benefits of exercise for MCI and dementia

Physical function. The improvement of motor functions may contribute to an improved health and quality of life for people with MCI and dementia. In people with MCI, exercise has been shown to improve strength (Nagamatsu, Handy, Hsu, Voss, & Liu-Ambrose, 2012; Tortosa-Martínez, Caus-Pertegaz, & Martínez-Canales, 2013), gait (Doi et al., 2013; Tortosa-Martínez et al., 2013), cardiovascular endurance (Baker & Frank, 2010; Tortosa-Martinez et al., 2015) and balance (Lam et al., 2011).

Exercise also has physical benefits for those that have already developed a dementia with programs that have been shown to be effective for improving cardiovascular endurance (Arkin, 2003; Sobol et al., 2016) strength (Steinberg, Leoutsakos, Podewils, & Lyketsos, 2009), mobility (Netz, Axelrad, & Argov, 2007; Toulotte, Fabre, Dangremont, Lensel, & Thévenon, 2003), speed of gait (Hageman & Thomas, 2002; Thomas & Hageman, 2003; Toulotte et al., 2003), flexibility (Toulotte et al., 2003), balance (Christofoletti et al., 2008; Toulotte et al., 2003), and ADL (Rolland et al., 2007; Santana-Sosa, Barriopedro, López-Mojares, Pérez, & Lucia, 2008; Venturelli, Scarsini, & Schena, 2011). For systematic reviews, see Blankevoort et al. (2010) and Lam et al. (2018).

Especially relevant are the benefits in ADL, as MCI and AD result in a progressive physical and cognitive deterioration that interferes with the capability of the person for performing these activities (Jefferson et al., 2008;

Martyr & Clare, 2012). This is a crucial problem in this population as the decrease in ADL performance increases dependency and is considered the main factor that reduces their quality of life (Andersen, Wittrup-Jensen, Lolk, Andersen, & Kragh-Sørensen, 2004). For this reason, interventions that slow down decline or improve ADL function are especially relevant. However, ADL not only depend on physical function but rely heavily on cognition, especially on executive functions (Martyr & Clare, 2012).

Cognitive benefits. Exercise seems to improve executive functions in people with MCI, such as selective attention, information search efficiency, processing speed, and cognitive flexibility (Baker & Frank, 2010; Lam et al., 2011; Logsdon, Mccurry, Pike, & Teri, 2009; Scherder et al., 2005; Tortosa-Martínez et al., 2015). Nagamatsu, Handy, Hsu, Voss and Liu-Ambrose (2012) also showed that a six-month strength training program improved selective attention and associative memory.

In people with dementia and AD, exercise programs have been shown to improve global cognition (Bossers et al., 2015; Cancela, Ayán, Varela, & Seijo, 2016), executive function (de Andrade et al., 2013; Bossers et al., 2015; Holthoff et al., 2015; Öhman et al., 2016), attention (de Andrade et al., 2013; Palleschi et al., 1996), visual attention and sustained memory (Yágüez, Shaw, Morris, & Matthews, 2011), visual and verbal memory (Bossers et al., 2015) or to attenuate cognitive deterioration (Arkin, 2003; Christofoletti et al., 2008; Kemoun & Roumagne, 2010; Venturelli et al., 2011). The mechanisms involved in the cognitive benefits associated with exercise remain unknown, with theories including increased cerebral blood volume and capillarization (Guiney, Lucas, Cotter, & Machado, 2015), levels of brain derived neurotrophic factors (de Assis & de Almondes, 2017) and hippocampal volume (Erickson et al., 2009; Griffin et al., 2011) or a decrease in oxidative stress (Radak et al., 2010), inflammatory processes (Cotman, Berchtold, & Christie, 2007), cardiovascular conditions (Mora, Cook, Buring, Ridker, & Lee, 2007; Mueller, 2007) or stress (Dijckmans et al., 2017; Tortosa-Martinez & Clow, 2012; Tortosa-Martínez, Manchado, Chulvi-Medrano, & Cortell-Tormo, 2018).

However, the cognitive benefits attributed to exercise for people with MCI and dementia remain controversial. A systematic review published by Gates, Fiatarone, Sachdev and Valenzuela (2013) concluded that the cognitive benefits of exercise in people with MCI was limited to the executive function (only verbal fluency), and that exercise did not benefit memory. Song, Yu, Li and Lei (2018) conducted a systematic review and meta-analysis concluding that exercise had a positive effect on overall cognition in people with MCI, although they were unable to find conclusive associations with specific-domain cognitive functions. Heyn, Abreu and Ottenbacher (2004), in another meta-analysis, found that an exercise intervention improved cognition in people with cognitive impairment and dementia.

In studies with only demented populations, a meta-analysis conducted by Smith et al. (2011) found that aerobic exercise training was associated with modest improvements in attention and processing speed, executive function, and memory. Groot et al. (2016) also performed a meta-analysis in which they concluded that aerobic exercise and combinations of aerobic exercise and strength training produce significant improvements in overall cognition accompanied by improvements in ADL in people with AD and other dementias. Guitar, Connelly, Nagamatsu, Orange and Muir-hunter (2018) performed a systematic review in which four out of the six studies reviewed found benefits in exercise (one intervention consisting in resistance training and three in combining aerobic with resistance training) for the executive function of people with AD. On the other hand, Forbes, Forbes, Blake, Thiessen and Forbes (2015) performed a Chochrane systematic review and found no significant cognitive benefits of exercise on cognition for people with dementia.

Neuropsychiatric symptoms. Neuropsychiatric symptoms (NPS) include mood disorders (depression, anxiety, euphoria and disinhibition), psychotic disorders (delirium and hallucinations) and behavioural problems such as agitation, aggressiveness and wandering (Spalletta et al., 2010). The frequency and intensity of these symptoms varies according to the type of dementia. People with AD generally present apathy, aberrant motor behaviour, irritability and delirium (Christofoletti et al., 2011). NPS are also present in MCI with a prevalence of up to 86% (Ellison, Harper, Berlow, & Zeranski, 2008).

NPS are key determinants for increased distress in patients and caregivers producing greater disability, worse quality of life, earlier institutionalization of the patients and increased burden for the caregiver (Lyketsos et al., 2011; McKeith & Cummings, 2005). Therefore, it should also be considered a main target for interventions.

Exercise involves potential benefits in the NPS in people with MCI although research is scarce. For example, Aman and Thomas (2009) showed the efficacy of an exercise program combining aerobic and strength training for reducing agitation in people with MCI. In a qualitative study, Tortosa-Martínez et al. (2017) showed that a three-month exercise program for people with amnestic MCI produced remarkable psychosocial benefits including improved mood, motivation, autonomy, perceived competence, self-esteem, and social relationships. The authors suggested that there are potential additional benefits of group exercise in this regard, as also suggested by Netz, Axelrad, Salit and Argov (2007) and in other populations such as women with fibromyalgia (Beltrán-Carrillo, Tortosa-Martínez, Jennings, & Sánchez, 2013).

In people with dementia, there are few studies that have showed promising results in mood (Arkin, 2003; Heyn, 2003; Williams & Tappen, 2007) and depression (Teri et al., 2003). The mechanisms mediating exercise benefits in mood and depression are not fully clear but it has been suggested that exercise may increase serotonin secretion (Ivy, Rodriguez, Garcia, Chen, & Russo-Neustadt, 2003).

There also some studies showing the benefits of exercise in decreasing aggression, agitation, delirium and passivity (Nascimento, Teixeira, Gobbi, & Stella, 2012). Scherder, Bogen, Eggermont, Hamers and Swaab (2010) proposed that these benefits could be a consequence of the effects of exercise on the amygdala and prefrontal cortex.

However, systematic reviews and meta-analysis on this topic show contradictory results. On the one hand, Forbes et al. (2015) did not find any associations between exercise and improvements in neuropsychiatric symptoms in people with dementia. On the other hand, more recently, Fleiner, Leucht, Förstl and Zijlstra (2017) concluded that exercise may improve behavioural and psychological symptoms in this same population.

METHODOLOGICAL GUIDELINES

The American College on Sports Medicine (ACSM) (Chodzko-Zajko et al., 2009a) and the World Health Organization (WHO, 2010) recommend a weekly minimum of 150 min of moderate-intensity aerobic or 75 min of vigorous-intensity aerobic activity with additional muscle-strengthening exercises, for overall health and to reduce the risk of cognitive decline in older adults. However, neither of them includes guidelines for the type, frequency and intensity of exercise recommended for people with dementia. Specific methodological guidelines for prescribing exercise for people with MCI or dementia are, thus, urgently needed. Although the current scientific evidence in this field of knowledge does not allow to establish firm conclusions about exercise prescription in this population, some preliminary guidelines might be taken into consideration.

The type of exercise might be aerobic, strength, balance and/or flexibility. Multimodal exercises are often prescribed and the combination of exercise with cognitive stimulation seems to be a trend.

Aerobic exercise. Aerobic exercise should be prescribed for older adults with cognitive impairment because of the potential benefits in physical function, cognition, depression, mood and behaviour associated with this type of exercise. There is not just one ideal type of aerobic exercise for older adults with cognitive impairment. As with healthy older adults, the best type of exercise will be prescribed individually according to the person´s medical record as well as previous exercise experience and preferences (Tortosa-Martínez, 2012).

The optimal intensity of aerobic exercise still needs to be fully clarified with evidence showing that light, moderate and high intensities might be beneficial. Most exercise prescription and research has focused on walking programs (Arkin, 2003; Venturelli et al., 2011; Winchester et al., 2013) or other mild intensity aerobic programs such as the study of Cancela et al. (2016), showing the benefits of a low intensity aerobic training on the cognitive functioning, behaviour, and functional mobility in people with dementia. The participants in this study cycled daily continuously for a minimum of 15 min at a constant self-selected pace in a recumbent bicycle with a very low resistance.

However, the trend seems to be prescribing higher intensities as they might produce higher adaptations. For instance, Baker and Frank (2010) designed a high intensity aerobic program in people with MCI that improved the participant´s executive function significantly, in particular selective attention, search information efficiency and cognitive flexibility. The program was followed for 6 months (4 days per week for 45 to 60 min per session). Participants exercised at 75% to 85% of the heart rate reserve (HRR), using a treadmill, stationary bicycle or elliptical trainer (at the person´s choice).

Similarly, Nagamatsu et al. (2013) found significant benefits of aerobic exercise on cognition for people with MCI. In this study, the initial intensity of the program was set at 40% of the HRR and was built up to the range of 70% to 80% of HRR. Participants also used the Borg's Rating of Perceived Exertion and the "talk" test for measuring the intensity.

Thus, the intensity of the exercise may be measured by estimations of the maximum heart rate either by an effort test (Baker & Frank 2010), the HRR (Nagamatsu et al., 2013), the Borg´s scale or the talk test (Nagamatsu et al., 2013). Adaptations of the Borg´s scale to a 1-10 range might be easier to understand. However, the efficacy of the rate of perceived exertion needs to be clarified in late stages of the disease.

The frequency of the aerobic exercise could be from daily to two days per week, even starting at one day per week according to the participant´s fitness level, and increasing the levels of physical activity gradually and slowly. It is recommended to first increase duration and frequency, and last the intensity.

Strength training. For people with dementia, it is common to observe muscle mass and strength losses. This will have a high risk for falls that may result in fractures as a consequence, especially during ambulation (Hageman & Thomas, 2002). Decreased muscle strength also decreases the ability to perform ADL, mobility, and predicts a lower life expectancy. Eventually, there is a loss of autonomy and a higher risk of institutionalization (Blankevoort et al., 2010). Hence, strength training is considered a relevant therapeutic intervention for any older adult to prevent frailty and dependence (Chodzko-Zajko et al., 2009b).

The potential utility of strength training for older adults with cognitive impairment is suggested not only for its beneficial effects on physical variables such as increased muscle mass and strength or increased balance, but also on cognition (memory and executive function).

The intensity of strength training needs to be at least moderate to achieve neuromuscular adaptations, with high intensity resistance training having proved to be safe and effective for people with MCI and dementia (Lindelöf, Karlsson, & Lundman, 2017; Nagamatsu et al., 2012). For cognitive benefits, it seems that performing strength training at this high intensity might be more beneficial (Bossers, Woude, Boersma, & Heuvelen, 2016; Chupel, Direito, Furtado, & Minuzzi, 2017; Fiatarone et al., 2014; Nagamatsu et al., 2012) while the effect of lower intensity resistance training combined with other exercise modalities was inconclusive in the systematic review of Gates et al. (2013).

For example, in the study of Fiatarone et al. (2014) the resistance exercise protocol included 3 sets of 8 repetitions of 5 to 6 exercises/session performed at high intensity involving most major muscle groups (chest press, leg press, seated row, standing hip abduction, knee extension) and using resistance training machines. Similarly, Nagamatsu et al. (2012) designed an exercise protocol also with resistance machines consisting of two sets of 6-8 repetitions of the following exercises: biceps curls, triceps extension, seated row, latissimus dorsi pull downs, leg press, hamstring curls, and calf raises. The training stimulus was increased gradually using the 7 Repetition Maximum (RM) method. Other exercises included minisquats, minilunges, and lunge walks.

In a study conducted by Chupel et al. (2017) a resistance exercise program using elastic bands promoted better anti-inflammatory balance and increased physical and cognitive performance in older women with cognitive impairment. The frequency of the program was two times per week during the initial 8 weeks increasing to three times per week during the following 12 weeks. The last 8 weeks of the program the frequency was again two times per week. The duration of each session was 45 min including the warm-up (5-10 min), main part (20-30 min) and the cool-down (5-10 min). The main part included 8-10 elastic band exercises using the yellow and red elastic bands (TheraBand, Hygenic Corporation, Akron, OH, USA). The exercise intensity was measured through the OMNI perceived exertion scale (PES), targeting 6-8 in the scale (corresponding to “somewhat hard” and “hard”). The number of sets progressed from 1 to 3 and the number of repetitions of each exercise varied from 10 to 12. The selected exercises were the front squat (standing or on a chair); unilateral hip flexion with chair; bench over row (with flexion); chest press (standing or on a chair); standing reverse fly; spine twist extension arm (obliques); shoulder press/twist arm front position; frontal total raiser; biceps arm curl (standing or on a chair); and overhead triceps extension.

In people with dementia, high intensity strength and functional training has been also proved to be effective and safe (Lindelöf et al., 2017; Toots et al., 2016). Lindelöf et al. (2017) propose a program performed in functional weight-bearing positions, including daily life movements such as squatting, walking over obstacles, reaching for objects while standing, and climbing stairs performed at an intended high intensity. The progression of the load is conducted by, for example, stepping higher, rising from a lower chair, or by adding weights onto a belt worn around the waist. High-intensity strength exercises are performed at 8 to 12 RM, increasing the load when the participant is capable of exceeding 12 repetitions in an exercise.

However, we should keep in mind that in order for strength training to be effective and safe, the technique of the exercises should be performed correctly, with the person being able to understand and follow instructions correctly. This is easier with people with MCI but may become more challenging when the cognitive impairment advances. In this regard, the ratio trainer/participants also needs to be considered. For example, in the Fiatarone et al. (2014) study this ratio was 1 trainer to 4-5 participants and in the study of Lindelöf et al. (2017) it was 2 trainers for 3 to 8 participants.

The control of the intensity could be carried out with estimations of the 1 RM (Fiatarone et al., 2014), the character of the effort (Lindelöf et al., 2017) or with effort perception scales (Chupel et al., 2017). In any case, the intensity should be gradually augmented, starting with an initial 30-40%.

The number of sets could progress from 1 to 3 and the number of repetitions will depend on the goal, just as with healthy older adults, usually ranging from 6 to 15. The frequency of the exercise should be one to three times per week with sessions of 20-40 min being effective (excluding warm-up and cool- down).

It has been suggested that the performance of ADL and potential risks such as falling, may be more closely associated with muscle power than with muscle strength and, therefore, strength training programs for the elderly should target muscle power (Cadore et al., 2014). Ramírez-Campillo et al. (2014) showed that a high-speed resistance training program produced greater improvements in muscle power and functional capacity in a sample of healthy elderly women. However, the effectiveness and safety of high-speed resistance training for older adults with cognitive impairment remains unknown and requires further research.

Strength training for older adults with cognitive impairment should target muscles involved in posture and gait. Changes in posture in older adults are associated with impaired mobility and the possibility of falls. These changes include greater kyphosis, internal rotation of the shoulder, a more posterior hip position (more anterior centre of gravity above the hips) (Woodhull-McNeal, 1992). We should then target muscles involved in posture such as core muscles, middle trapezius, rhomboids or posterior deltoids.

Dementia is also characterized by gait deterioration causing an increased risk of falls (Ijmker & Lamoth, 2012). In fact, quantitative gait dysfunction is a predictor of cognitive decline and higher risk of developing dementia (Verghese, Wang, Lipton, Holtzer, & Xue, 2007). Thus, muscles involved in gait such as biceps femoris, quadriceps, rotators of the hip, gastrocnemius and anterior tibial should also be targeted.

There are several options in terms of the equipment used in strength training such as using one´s body, free weights, elastic bands or resistance training machines. The use of free weights is probably not the best option in late stages of the disease, and it is desirable to avoid lifting weights above the shoulders to avoid injuries (Rimmer & Smith, 2009). Group strength exercises may be also performed such as, for instance, two participants holding a ring pulling in opposite directions (Netz et al., 2007).

Finally, one possible type of strength training that needs to be studied is isometric training (Hess & Smart, 2017). The meta-analysis of Cornelissen and Smart (2013) showed that 4 sets of 2 min of isometric strength training performed at 20-50% of maximal voluntary isometric contraction may produce a significant reduction in blood pressure in hypertensive, prehypertensive and normal blood pressure subjects. Furthermore, these benefits were higher than those shown with aerobic training or dynamic strength training. Considering that a poor cardiovascular health is one of the main risk factors for developing dementia, and the feasibility of this type of training for older adults, this modality of strength training should be analysed in future studies (Hess & Smart, 2017).

Balance training. The incidence of falls is two to three times (Horiwaka et al., 2005) or even nearly eight times greater in older people with dementia than in healthy older adults causing functional limitation, loss of independence, loss of confidence, associated illness and mortality in this population (Allan, Ballard, Rowan, & Kenny, 2009). Furthermore, falls could lead to head trauma and stroke which are known to be a risk factor for dementia and may also worsen cognitive impairment (Li et al., 2017).

Poor balance is a major contributor of falls (Russell, Hill, Blackberry, Day, & Dharmage, 2006), and a decline in balance is a common characteristic in people with cognitive impairment and Alzheimer's disease (Pettersson, Engardt, &

Wahlund, 2002). Therefore, exercise programs for people with cognitive impairment should consider balance as an essential component.

The recent meta-analysis conducted by Lam et al. (2018) reported a significant improvement with exercise in balance as measured by the Berg Balance Scale by 3.6 points (95% CI 0.3 to 7.0). The systematic review of Suttanon, Hill, Said and Dodd (2010) showed that balance programs for people with dementia involved generally combined exercises including flexibility, strengthening, walking and balance components. The frequency of the balance programmes ranged from twice a week to twice a day, with 30 to 60 min per session.

Different exercises can be implemented for balance training such as shifting centre of gravity, tandem walks, forward and backward walks, and chair sit to stands (Steinberg et al., 2009); walking on a variety of surfaces and standing positions on one leg (Toulotte et al., 2003); walking while changing directions (Netz et al., 2007); or games and activities with equipment (e.g. cones, hoops, foam rubber sheets or Swiss balls) (Suttanon et al., 2010).

The difficulty of the exercises should be increased gradually. Few studies have reported the progression criteria for balance exercises with only one study (Shaw et al., 2003) included in the Suttanon et al. (2010) review. In this study, the progression was set over four levels (1 to 4) that corresponded to progressively decreasing support and increasing manoeuvrability during standing balance activities. Lindelöf et al. (2017) proposed that high-intensity balance exercises should fully challenge postural stability and progress by narrowing the base of support, altering the surface, or performing more challenging exercises. Nevertheless, until more detailed guidelines are recommended for the progression of balance programs we could follow the general guidelines established by the ACSM (Chodzko-Zajko et al., 2009a) for training balance in older adults: 1) reduce the base of support (e.g. two-legged stand, semi-tandem stand, tandem stand, one-legged stand); 2) use dynamic exercises that alter the center of gravity (e.g. tandem walk, circle turns); 3) target postural muscle groups (e.g. heel stands, toe stands); 4) change the sensory input (e.g. standing with eyes closed).

Last, when designing balance programs for older adults with cognitive impairment, dual-task training may be a useful strategy as older adults with a poor performance under dual tasks have an increased risk of falling. Dual-task is also related to ADL as many of these activities require concurrent performance of two or more tasks. Dual-task training consists in performing two or more cognitive and motor activities at the same time while maintaining postural control. Dual-task training should be, thus, an essential component of fall prevention programs in older adults (Silsupadol, Siu, Shumway-Cook, & Woollacott, 2006). However, although dual-task training has been proved to be effective in improving dual-task conditions in people with dementia (Schwenk, Zieschang, Oster, & Hauer, 2010), the efficacy of this type of training for improving balance and reducing the risk of falls still needs to be determined in this population.

In any case, balance programs for people with cognitive impairment need some adaptations in regard to the duration, frequency and type of exercise, compared to those for healthy older adults, in order to accommodate the specific balance impairments and tasks that can be performed safely by people with cognitive impairment (Suttanon et al., 2010).

Flexibility training. Flexibility training should be also considered in exercise programs for older adults. The ACSM (Chodzko-Zajko et al., 2009a) recommends a frequency of at least two days per week with a moderate intensity. Static stretches sustained for 30 to 60 s for major muscles groups. It is also important to stretch postural muscle groups that might be shortened, such as the pectoralis major, the latissimus dorsi, the anterior deltoids, the psoas and quadriceps. Avoid exercises that require getting down or up from the floor as it will be difficult for many participants (Rimmer & Smith, 2009). Emphasize breathing techniques during stretching to promote relaxation. This could reduce stress and agitation.

Multi-modal exercise. Individuals with MCI and dementia present difficulties in cognitive as well as motor domains that affect their quality of life. Therefore, the use of isolated interventions may be insufficient given the complex and multifactorial nature of the disease (Fissler, Küster, Schlee, & Kolassa, 2013) and the different adaptations to different exercise modalities. Nevertheless, Schneider & Yvon (2013) critiqued that the interventions offered to people with cognitive impairment many times had the only objective of impacting cognitive performance, recommending programs that include multiple types of intervention.

Furthermore, Smith et al. (2010) suggested after performing a meta-analysis, that exercise interventions including different exercise modalities such as combinations of aerobic and strength training could be more effective even for cognitive aspects. Very recently, Guitar et al. (2018) also showed in their systematic review that combined physical exercise interventions (i.e. an exercise program with aerobic, strength training, and flexibility or balance components), reported statistically significant improvements in executive function.

Multimodal training has also been proved effective for improving neuropsychiatric symptoms. For example, Hoffmann, Sobol, Frederiksen, Beyer and Vogel (2016) reported that 16 weeks of combined strength and aerobic training significantly decreased neuropsychiatric symptoms and improved cognition in those patients with higher attendance and intensity of the exercise. The exercise was performed in a ratio of 2-5 participants per trainer. The first month was dedicated to adaptation to the exercise and building up strength, especially in the lower limbs (twice weekly), and introduction to aerobic exercise (once per week). For the rest of the program a moderate to high intensity (70–80% of maximal heart rate calculated as 220 - the person's age) aerobic interval training was performed (in total 3 × 10 min on an ergometer bicycle, cross trainer, and treadmill with 2–5 min rest in between).

ADL may also be improved with combinations of different exercise modalities. Santana-Sosa et al. (2008) designed an exercise program for people with AD combining strength training, joint mobility and coordination exercises which improved the participants´ global functionality and their performance in ADL independently, such as walking, standing from a chair, changing from a chair to the bed, bathing or dressing up. More recently, Bossers et al. (2016) showed that a combination of aerobic and strength training (two walking session and two strength training sessions of 30 min per week) was more effective to target ADL dysfunction compared to aerobic training alone (four walking sessions per week).

When performing multimodal exercise programs that combine aerobic and strength training (concurrent training), the guidelines provided by Cadore and Izquierdo (2013) for healthy older adults could be followed. These authors conclude that concurrent training is the most effective strategy for improving neuromuscular, cardiorespiratory functions, and functional capacity in healthy older adults, despite the interference effect on strength gains that is caused by this combined training. They suggest three sessions per week, performing strength prior to endurance exercise, to optimize both neuromuscular and cardiovascular gains.

Combining exercise with cognitive stimulation. It has been suggested that the cognitive benefits elicited by physical activity can be increased by adding exposure to a cognitively challenging environment (Karssemeijer et al., 2017; Zhu, Yin, Lang, He, & Li, 2016). The cognitive activity may be performed in a different session to the physical activity (sequentially) or at the same time (simultaneously). Simultaneous programs could be performing cognitive activities intrinsic to the exercise or separate but performed at the same time of the exercise. Sequential interventions consist on having two separate sessions, one for the exercise training and one for the cognitive training. It has the disadvantage of increasing the time necessary for training and it may reduce the potential synergies between the two training types (Schneider & Yvon, 2013; Teixeira et al., 2012).

Simultaneous interventions seem to be more effective and are, for example, cycling while performing cognitive exercises presented on a screen (Yoon et al., 2013). Exergaming is a good example, which provides cognitive stimulation with virtual reality tours when taking part in, for instance, stationary cycling (Anderson-hanley et al., 2012). Neuro-exergaming is a novel option that has been proved more effective than exergaming in healthy older adults by Anderson-hanley et al. (2018), which consisted in their study of pedalling and steering a stationary bike along a virtual bike path to achieve a predetermined target heart rate while playing a computer game designed to stimulate cognition.

Zhu et al. (2016) conducted a meta-analysis showing significant benefits on overall cognitive function of combined exercise and cognitive stimulation compared to exercise training alone or a control group in healthy older adults. More specifically, combined programs induced significant improvements with moderate effect sizes for global cognitive function and visuospatial ability, and small effects for memory, executive function and attention. In people with MCI and dementia, the meta-analysis of Karssemeijer et al. (2017) revealed the significant benefits of combined cognitive and physical interventions, compared with both single exercise training and a control group, on global cognitive function, ADL and mood. However, the results of this study did not show a significant effect on the specific cognitive domains of executive function/attention and memory. Very recently, Donnezan, Perrot, Belleville, Bloch and Kemoun (2018) in a randomized controlled trial with people with amnestic MCI showed larger benefits in executive function of aerobic training combined with cognitive stimulation compared to physical training only or cognitive training only.

There is also a lack of methodological guidelines for combining physical and cognitive training, especially when the cognitive stimulation is inherent to the physical exercise. These interventions require an interdisciplinary approach, with exercise science professionals, psychologists and neurologists working closely together.

Other methodological considerations. Exercise programs should be conducted by qualified exercise science professionals with a specific training in cognitive impairment (Tortosa-Martínez et al., 2017). The participants should get medical clearance before engaging in the exercise program (Tortosa-Martínez, 2012). An interdisciplinary approach between exercise professionals, neurologists and psychologists should be the main focus for the adequate design and implementation of high-quality exercise programs (Tortosa-Martínez et al., 2017). Rimmer and Smith (2009) suggested that exercise programs should be performed preferably in the morning, as people with cognitive impairment usually have a higher level of agitation, fatigue and tiredness at the end of the day.

In order to promote adherence, perceived competence and autonomy, as well as enhancing the psychosocial benefits, exercise programs should be designed considering the following (Tortosa-Martínez et al., 2012, 2017):

(1) To perform group-based exercise if possible, promoting cooperation, interaction and physical contact of all participants in equal status. In any case, previous exercise experience and preferences need to be taken into account. To promote humour, fun and a positive social atmosphere. In this regard, consider including short simple games in the sessions.

(2) To keep control and follow-up of attendance, making phone calls when somebody misses a session. The schedule, and any changes made, should be available to the participants and caregivers in a written document.

(3) Instructors should show an attentive, respectful, caring and warm attitude. A friendly welcome and farewell should be included as a part of the session structure.

(4) To implicate caregivers in the program and invite them to participate in the exercise program. Also, to plan recreational activities out of the program (e.g. a meal). To give information to the participants and caregivers about the benefits of exercise. To create a link and a sense of belonging to the group.

(5) Positive feedback is especially important, giving verbal explanations linked to action, using non-verbal language and using modelling only in case it is really necessary because the promotion of personal autonomy should be a focus of the program. Spatial orientation feedbacks are especially relevant. When performing movements around the space, permanent, intermittent or occasional support (depending on the person) should be provided. Working in pairs can be a useful tool for this support.

(6) To propose exercises according to the participants' level of physical and cognitive functionality deficits and to provide enough time to learn new activities with progressive learning processes (from less to more difficulty). In case of exercises with a higher degree of difficulty, break down the exercise in parts, repeat the parts and finally integrate them. New exercises should be presented previously and linked with other exercises through space and equipment.

(7) The adaptation of activities needs to be individualized in the action, according to the progression of the disease, and providing a space for personal adaptations if necessary. However, keep in mind that the best adaptation is the one that is effective but not perceived.

(8) It is important to follow safety standards and look for safe environments, avoiding objects that may cause falls and excessive visual or

auditory stimulation, as it may cause orienteering problems and/or agitation to some individuals, especially with higher degrees of cognitive impairment.

Conclusions

Exercise seems to be an effective strategy for preventing dementia, slowing down the progression of the disease and improving the quality of life of those already affected by it. Multimodal programs, including aerobic, strength, balance and flexibility training, designed according to the participants´ level of physical and cognitive functionality, seem to be the best approach. The frequency of the program should be from 2 to 4 days per week, with an initial mild intensity but gradually progressing to moderate and high intensities. However, more research is needed in order to prescribe safe and efficient exercises for this population.

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